REMARKS

FORMAL MATTERS:

Claims 27, 31, 32, 34-38, 46-49, 52-82 are pending after entry of the amendments set forth herein.

Claims 50 and 51 are canceled without prejudice.

Claims 46-49, 52, and 79-82 stand withdrawn as being directed to non-elected subject matter.

Claims 27, 31, 55, 59, 63, 67, 71 and 75 are amended. Claims 59, 67 and 75 are amended to correct antecedence. Support for amendments to Claims 31 and 63 may be found at page 13, line 13 and at page 5, lines 16-19. Support for the amendments to Claims 27, 31, 55, 63, and 71 may be found throughout the specification, at for example page 10, lines 9-10; page 25, lines 3-10; page 26, lines 1-5; and by example, page 47-48.

Claims 79-82 are added. These claims find support in, for example, claims 46-49 and 52 as originally filed.

No new matter is added. As such, the Examiner is requested to enter the above amendments.

INTERVIEW SUMMARY:

Applicant thanks Examiner Le for the courtesy of conducting an in-person interview on September 1, 2009 with Applicant's representative Carol Francis to discuss the rejections in the Final Office Action. Applicant's representative, Elizabeth Alcamo, attended by telephone. Peter Brazier, of the assignee NewBiomed PIKA Pte Ltd, also attended by telephone.

The rejections as set out in the Final Office Action dated July 31, 2009 were discussed, including the rejections under §112, ¶1 (new matter), §103(a), and for obviousness-type double patenting. Applicant proposed claim amendments and presented arguments during the interview, which amendments and arguments are presented herein.

INFORMATION DISCLOSURE STATEMENT:

The Applicant notes that an Information Disclosure Statement (IDS), including an SB/08A form, is submitted herewith. The Applicant respectfully requests that the Examiner initial and return this SB/08A form, thereby indicating that the references cited in the IDS have been reviewed and made of record. For the Examiners convenience, a copy of this form is enclosed herewith.

STATEMENT UNDER 37 C.F.R. §§1.56 AND 1.2

Applicant hereby advises the Examiner of the status of a co-pending application in compliance with the Applicant's duty to disclose under 37 C.F.R. §§1.56 and 1.2 (see also MPEP §2001.06(b)) as discussed in *McKesson Info. Soln. Inc., v. Bridge Medical Inc.*, 487 F.3d 897; 82 USPQ2d 1865 (Fed. Cir. 2007).

The Applicant wishes to bring to the Examiner's attention the following:

- a Response to a Final Office Action was mailed on August 28, 2009 in copending U.S. Patent Application No. 11/331,575 (NBMP-002), filed January 13, 2006;
- A Response to a Final Office Action was mailed on August 11, 2009 in co-pending U.S. Patent Application No. 11/331,839 (NBMP-003), filed January 13, 2006;

These documents are available on PAIR, and thus are not provided with this communication.

REJECTIONS UNDER §112, ¶2

Claims 59, 67 and 75 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 59, 67 and 75 were rejected for recitation of the limitation "the rabies antigen" on the grounds that there is insufficient antecedent basis for this limitation in the claim.

Claims 59, 67 and 75 are amended to correct antecedence. Reconsideration and withdrawal of this rejection is requested.

REJECTIONS UNDER §112, ¶1

Claims 31-38, 52-54 and 63-70 rejected on grounds that the claims require that the polynucleotide adjuvant composition have an average molecular size "equal to " 13.5S and 15S, but that written support does not exist for the cited limitation "equal to". This rejection is traversed as applied and as it may be applied to the currently pending claims. Each of these rejections is addressed in turn below.

It is well-established that a numerical range provides written description support for the range, as well the end points of the range.[1]

Claims 31 and 63 are amended to recite "about or greater than 338,000 Daltons" and "about or greater than 13.5 Svedbergs". The specification at page 13, line 13 provides support for "about 13.5 Svedbergs" since this numerical value appears as an endpoint of this range. Guidance for calculating average molecular weight from average molecular size at page 5, lines 16-19. Using this formula and "about or greater than 13. 5 Svedbergs", one arrives at "about or greater than 338,000 Daltons".

As to Claim 32, the specification at page 10, line 25 – page 11, line 2 recites that the composition molecules may have "an average molecular weight . . . equal to or greater than 500,000 Daltons". Again, using the guidance on calculating average molecular size from average molecular weight at page 5, lines 16-19 of the specification and the value "equal to or greater than 500,000 Daltons", one arrives at "equal to or greater than 15 Svedbergs".

Withdrawal of these rejections of the claims is respectfully requested.

[1] *In re Wertheim*, 541 F.2d 257 (CCPA 1976)

REJECTIONS UNDER §103(A)

Claims 27, 31-32, 34-47 and 52-54 rejected under § 103(a) as being unpatentable over Zong et al.[2] as evidenced by Lin et al.[3] in view of Morahan et al.[4] The Examiner asserts that arriving at the present invention is "routine optimization." This rejection is respectfully traversed as applied and as it may be applied to the claims as presently pending.

The Court in *KSR* repeatedly emphasized that an obviousness inquiry must take into account the predictability of the field:[5]

> If a person of ordinary skill can implement a predictable variation, §103 likely bars its patentability. For the same reason, if a technique has been used to improve one device, and a person of ordinary skill in the art would recognize that it would improve similar devices in the same way, using the technique is obvious unless its actual application is beyond his or her skill. *Sakraida* and *Anderson's-Black Rock* are illustrative—a court must ask whether the improvement is more than the predictable use of prior art elements according to their established functions.

(emphasis added)

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[2] Zong et al. (1993) "Study on Determining the Molecular Weight of PICKCa and PI.PC with the Method of Polyacrylamide Gel Electrophoresis (PAGE)" *Chinese Journal of Pharm. Analysis* 13 (4): 219-222. (Applicants note that the reference's first author is "Zong Jianchao", and thus Zong is the author's first name. However, for sake of consistency in the file history, this reference is referred to as "Zong et al.")

[3] Lin et al. (1993) "A New Immunostimulatory Complex PICKCa in experimental rabies: antiviral and adjuvant effects." *Archives of Virology* 131(3-4):307-319.

[4] Morahan et al. (1972) "Antiviral Activity and Side Effects of Polyriboinosinic-Cytidylic Acid Complexes as Affected by Molecular Size" *Proc. Natl. Acad. Sci.* 69(4): 842-846.

[5] *KSR International Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1740 (US 2007) (citations omitted).

Furthermore, when considering the Federal Circuit's application of the "obvious to try" standard to the adjustable gas pedal invention at issue, the Court stated:[6]

> When there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under §103.

(emphasis added)

After the decision in *KSR*, the Office promulgated examination guidelines on determination of obviousness, when office personnel reject claims by attempting to combine prior art elements according to allegedly known methods to yield predictable results, the Office must resolve the *Graham* factual inquiries and articulate, in part, "a finding that one of ordinary skill in the art would have recognized that the results of the combination were predictable."[7]

We now turn to an analysis of the rejection as it may be applicable to the presently pending claims.

The problems to be solved is providing an adjuvant composition suitable for use in humans

At least two problems must be addressed in developing an adjuvant composition, particularly where that adjuvant composition is to be suitable for use in humans. Such adjuvant compositions must have a balance between (1) immunogenicity; and (2) toxicity. For example:

- If an adjuvant is found to have good immunogenicity, but at the same time exhibits toxicity that renders it unsuitable for human administration, then the adjuvant is unacceptable for human use.

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[6] *KSR*, 127 S. Ct. at 1747.

- If an adjuvant has a sufficiently low toxicity that gives it a good safety profile (i.e., making it suitable for administration to humans), but at the same time has relatively low immunogenicity, then the adjuvant is not of interest.

The Office has taken the position that the claimed compositions are obvious based on the combined disclosures of Zong et al. (as evidenced by Lin) in view of Morahan. However, as evidenced below, the ordinarily skilled artisan would not look to Morahan, which describes a poly IC adjuvant composition, in order to provide an adjuvant composition suitable for use in humans.

The ordinarily skilled artisan would not look to Morahan for guidance on optimization of an adjuvant suitable for use in humans since Poly IC does not have adjuvant activity in humans.

As discussed during the interview, Poly IC adjuvants (such as those described by Morahan) have not been commercialized for use in humans as they have been found to be generally ineffective as an adjuvant in humans, e.g., due to degradation by nuclease present in human plasma (see, e.g., specification, page 4, lines 1-2) and due to toxicity in preclinical studies (as discussed in specification, page 3, lines 19-28).

In support of this position, Applicants provide here a publication by De Clercq[8] (Exhibit A). De Clercq was published in 1979, before the priority date of the present application but after the 1972 publication of Morahan. De Clercq teaches that human sera represses interferon response to Poly IC:[9]

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[7] "Examination Guidelines for Determining Obviousness Under 35 U.S.C. 103 in View of the Supreme Court Decision in *KSR International Co. v. Teleflex Inc. Federal Register* 72 (10 Oct. 2007) 57526-57535, at 57529 (*citing KSR International Co. v. Teleflex Inc.*, 127 S. Ct. 1727 (US 2007).

[8] De Clercq (1979) ":Degradation of Poly(inosinic acid) – poly(cytidylic acid) [$(I)_n$ $(C)_n$] by Human Plasma"· *Eur. J. Biochem.* 93:165-172.

[9] De Clercq, page 165, col. 2, first full paragraph.

> It was further demonstrated that human plasma (serum) contains high concentrations of an enzyme that hydrolyzes [13], and thereby inactivates [14], $(I)_n \cdot (C)_n$. By and large, those animal species that show a large capacity to hydrolyze $(I)_n \cdot (C)_n$ poorly respond to the interferon-inducing activity of $(I)_n \cdot (C)_n$, whereas those species that are good responders have low hydrolyzing capacity [15]. Even when transferred to mice, human serum and various other sera were found to suppress the interferon response to $(I)_n \cdot (C)_n$; this inhibitory activity was attributed to the ribonuclease content of the serum [16].

(emphasis added)

De Clercq also provides an explanation as to why Poly IC performs so poorly as an adjuvant, demonstrating that the half-life of poly IC is only about 6 min in 50% human plasma:[10]

> Degradation of $(I)_n \cdot [^3H](C)_n$ by human plasma proceeded very quickly: the time required to reduce acid-insoluble radioactivity by 50% varied from 3 min to 20 min, depending on the total $(I)_n \cdot (C)_n$ concentration (Fig. 2). For a total $(I)_n \cdot (C)_n$ concentration of 1 μg/ml, degradation was almost complete after 10 min incubation (in the presence of 50% plasma). For an $(I)_n \cdot (C)_n$ concentration of 10 μg/ml, that is the plasma $(I)_n \cdot (C)_n$ level that could be attained if $(I)_n \cdot (C)_n$ is administered to human beings at the highest feasible dose (10 mg/kg [8,10]), the half-life of $(I)_n \cdot (C)_n$ in the presence of 50% human plasma was only 6 min (Fig. 2). When $(I)_n \cdot [^3H](C)_n$ (0.6 μg/ml) was assayed in the presence of 2% human serum, its half-life was approximately 20 min [23].

(emphasis added)

To overcome the stability problems of Poly IC adjuvants, modified forms of Poly IC, such as Poly ICLC and PICKCa, have been developed.[11] The compositions are referred to herein for convenience as "PIC-containing compositions". The chemical composition in PIC-containing compositions is generally designed to enhance the stability of the Poly IC structure. De Clercq

[10] De Clercq, page 167, col. 1, first full paragraph.

[11] See, e.g., specification, page 4, lines 2-14.

notes that PIC-containing compositions that are more resistant to plasma nucleases would be attractive, but at the same time warns that such compositions could have issues with toxicity:[12]

> As they are more resistant to degradation by plasma nucleases, $(I)_n \cdot (br^5C)_n$ and $(I)_n \cdot (s^2C)_n$ should persist longer in plasma (and other biological fluids), and may, therefore, be expected to be more efficient as interferon inducers than $(I)_n \cdot (C)_n$ when administered to man. However, by virtue of their prolonged persistence in biological fluids $(I)_n \cdot (br^5C)_n$ and $(I)_n \cdot (s^2C)_n$ may also be more efficient in inducing other, possibly noxious, physiological responses. The same argument does, of course, apply to the $(I)_n \cdot (C)_n$ · poly-L-lysine · carboxymethylcellulose complex (referred to in the introduction, see also [17—19]).

Thus, such PIC-containing compositions still face the problem of finding the immunogenicity-toxicity balance described above in order to be suitable for administration to humans.

The art in the area of PIC-containing compositions teaches that increasing molecular weight/ size of PIC-containing compositions increases toxicity, and thus, lower molecular weights/sizes are more suitable for use in humans.

Should the ordinarily skilled artisan turn to the literature in the area of PIC-containing compositions for guidance on modification of the polynucleotide adjuvant of Zong et al., he would find that the art teaches that increasing molecular weight/size of the PIC of a PIC-containing composition increases toxicity, thus decreasing the compositions suitability for use in humans. Accordingly, one of ordinary skill in the art would aim for PIC-containing compositions comprising smaller molecular weight/size PIC. Applicant provides the following examples.

Gatmaitan et al[13]

Gatmaitan et al. (Exhibit B) describes a study of Poly ICLC, a PIC-containing composition composed of Poly IC complexed with poly-L-lysine and carboxymethcylcellulose.

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[12] De Clercq, page 171, col. 1, second full paragraph.

[13] Gatmaitan et al. (1980) "Modified Polyriboinosinic-Polyribocytidylic Acid Complex: Induction of Serum Interferon, Fever, and Hypotension in Rabbits" *Antimicrobial Agents and Chemotherapy* 17:49-54.

This modified complex is more resistant to nucleases in primate serum than Poly IC.[14] In view of the fever and significant drop in blood pressure (hypotension) observed as side effects in some patients who received Poly ICLC during a human clinical trial, Gatmaitan et al. conducted a study in rabbits.[15] The results of their experiments are summarized in Table 1, which is reproduced below:[16]

TABLE 1. *Serum interferon, febrile and hypotensive responses in rabbits after administration of poly ICLC (9S) or poly ICLC (4S) to rabbits*

Procedure	Serum interferon	Fever	Hypotension
Normal saline, i.v.	None	None	None
Hydrocortisone i.v.	None	None	None
→ poly ICLC (9S), i.v.	Marked	Marked	Marked
poly ICLC (9S), i.v. followed by HC,* i.v.	Moderate	Moderate	Moderate
HC, i.v. followed by poly ICLC (9S), i.v.	Minimal	None	None
poly ICLC (9S), i.m.	Minimal	Marked	None
poly ICLC (9S), s.c.	Minimal	Marked	None
→ poly ICLC (4S), i.v.	Marked to moderate	Marked	None
poly ICLC (4S), i.m.	Minimal	Marked	None

* HC, hydrocortisone.

(emphasis added)

Notably, a larger Poly ICLC (9S) administered intravenously elicited a "marked" interferon response, but at the same time caused marked fever and hypotension. In contrast, a smaller Poly ICLC (4S) administered by this same route elicited "marked to moderate" interferon response, but no hypotension. In view of this data, the ordinarily skilled artisan would conclude that PIC-containing compositions such as Poly ICLC exhibit increasing toxicity with increasing size, and would expect that *increasing size of the composition of Zong et al. would also result in increased toxicity.*

***Levy et al.*[17]**

Levy et al. (Exhibit C) describes additional analysis of toxicity of Poly ICLC in mice, which the authors summarize in Table 1:[18]

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[14] Gatmaitan et al. at page 49, col. 1, first full paragraph.

[15] Gatmaitan et al. at page 49, paragraph bridging cols. 1 and 2.

[16] Gatmaitan et al., at page 53.

[17] Levy et al., (1981) "Interferon Induction in Primates by Stabilized Polyriboinosinic Acid-Polyribocytidylic Acid: Effect of Component Size" *Infect. Immun.* 34:416-421.

[18] Levy et al. at page 420, col. 2.

TABLE 1. *Toxicity in mice of poly(I)·poly(C) and poly(ICLC) complexes administered by different routes*[a]

Drug	LD_{50} (mg/kg)	
	i.v.	i.p.
9S poly(ICLC), 27,000 plL[b]	12.5	13.8
6S poly(ICLC), 27,000 plL	15.0	25.0
4S poly(ICLC), 27,000 plL	25.0	40.0
9S poly(I)·poly(C)	30.0	45.0
9S poly(ICLC), 2,000 plL	26.0	
9S poly(ICLC), 3,400 plL	25.0	
9S poly(ICLC), 13,000 plL	15.0	

[a] Five groups of 20 mice per group were injected with either 10, 20, 30, or 40 mg of each of the complexes per kg. The animals were observed for 2 weeks. Fifty percent lethal dose (LD_{50}) values were calculated by the method of Reed and Muench (5).
[b] Molecular weight of polylysine (plL).

(emphasis added)

As indicated above, the median lethal dose (LD_{50}) for intravenous or intraperitoneal administration of poly ICLC is correlated with molecular size, with the smallest LD_{50} associated with the largest Poly ICLC and the highest LD_{50} associated with the smallest Poly ICLC. In other words, 9S Poly ICLC was the most toxic and 4S Poly ICLC was the least toxic of the molecular sizes tested. Thus, Poly ICLC exhibited a correlation between molecular size and toxicity, such that the lower molecular size was less toxic. Thus, Levy et al., like Gatmaitan et al., points away from using PIC-containing compositions with PIC of larger molecular weight/size and in favor of PIC-containing compositions with PICs of lower molecular weight/size in order to avoid toxicity.

Shu et al.[19]

Shu et al. (Exhibit D) describes a PIC-containing composition referred to as "PICKCa", which contains Poly IC, kanamycin and calcium:[20]

[19] Shu et al. (1989) "Biological functions and application of Poly I:C" *Shanxi Journal of Medicine* 18(10):40-42.

[20] Shu et al. English translation at page 1, 2nd full paragraph.

> It is believed that the molecular weight of PIC is related to its biological functions. In the serum of mice, the duration time of induced IFN production was elongated along with the increasing molecular weight of PIC. **Molecular weight is related to toxicity, which has restricted the clinical application of PIC**. To overcome the above shortages, scientists switched the focus from pure PIC or mother PIC to compound and modified PIC, and later several similar derivants were discovered. **PIC product in our country is a kind of new compound which is made by adding a few kanmycin and CaCl2 to PIC.** The precise name should be PICKca or poly I:Ckca. It was observed by electron microscopy that kanmycin and CaCl2 formed network linking PIC short chains to be long chains and enhancing stability and binding capability of PIC to cells.

(emphasis added; typographical errors original to English translation)

Shu et al. further indicate that PICKCa (described as "Domestic PIC" below) is suitable for use in humans, and that its safety is attributable to its lower molecular size:[21]

> The toxicity of PIC is somehow related to its molecular weight, dose, delivery route and therapeutic target. **Domestic PIC has a low molecular weight, for instance, the Tianjin PIC is 6s on average (4-12s),** and low dose (50 fold less than that in foreign countries, i.e. 0.02-0.08 mg/kg).

(emphasis added)

Thus, Shu et al. teaches that lower molecular weights/sizes of PIC in PICKCa, e.g. 4S to 12S, and on average 6S, provide for lower toxicity. Thus, Shu et al. teaches that a PICKCa of a *smaller* size is desirable to provide an adjuvant suitable for use in humans.

The Claimed Invention

Despite the direction in the art relating to PIC-containing compositions such as PICLC and PICKCa to make compositions of lower molecular weight/size, the inventor of the present claims found that the claimed polynucleotide adjuvant having a *greater* molecular weight/size exhibited the desired balance of immunogenicity and toxicity that rendered it suitable for human use. Examples 7 – 10 of the above-referenced specification illustrate that, in contrast with PIC

[21] Shu et al. English translation page 3, fourth paragraph.

and Poly ICLC, "PIKA" of the claimed invention remains well tolerated at high molecular weight.

Conclusion

As evidenced by De Clercq, Poly IC compositions such as those described in Morahan are rapidly degraded in human plasma, and thus do not provide the necessary adjuvant activity in humans. Accordingly, the ordinarily skilled artisan would not look to Morahan for guidance for size and molecular weight characteristics of the claimed adjuvant composition (referred to herein as "PIKA").

The skilled artisan would instead turn to the art of PIC-containing compositions, which were developed to solve the degradation problems of Poly IC compositions. However, if the skilled artisan were to turn to this art for guidance on optimization of Zong to achieve a balance of adjuvant activity and toxicity in an adjuvant composition suitable for use in humans, the art as exemplified above would point the ordinarily skilled artisan toward making compositions of *smaller* molecular weight/size than those of the present claims. In contrast, and unexpectedly, the inventor has found that "PIKA" having a *larger* molecular weight/size as recited in the present claims provides an adjuvant suitable for human use – it unexpectedly exhibits enhanced immunogenic adjuvant activity *without* a concomitant increase in toxicity.

Thus, the claimed adjuvant compositions do not represent implementation of a predictable variation by modification of molecular weight/size of the composition of Zong et al. that is in accordance with the teaching in the art. Stated differently, *increasing* the molecular size and weight of the claimed compositions is not "a technique [that] has been used to improve one device, and a person of ordinary skill in the art would recognize that it would improve similar devices in the same way."[22] Indeed, as exemplified above, the art in the area of PIC-containing compositions teaches that as molecular weight/size increases, so does the toxicity of the composition. Thus, the ordinarily skilled artisan looking to providing an adjuvant suitable for human use would expect that increasing molecular weight/size of the claimed "PIKA" composition would also cause toxicity to increase so that it was not suitable for use in humans. Surprisingly, and as illustrated in the specification, increasing the molecular size and molecular

[22] *KSR,* 127 S.Ct. at 1740.

weight of the claimed "PIKA" compositions provided an adjuvant composition that was both effective in its adjuvant activity *and* exhibited a toxicity profile suitable for use in humans. See, e.g., specification Examples 7 – 13, specification pages 45 – 52.

Reconsideration and withdrawal of this rejection of the claims is respectfully requested.

REJECTION UNDER §103(A) – ZONG IN VIEW OF MORAHAN AND LIN ET AL.

Claims 27, 31-32, 38 and 55-78 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Zong et al., in view of Morahan et al., as applied in Rejection I, in further view of Lin et al. The Examiner asserts that Lin et al. teaches inclusion of an antigenic compound. This rejection is respectfully traversed as applied, and as it may be applied to the currently pending claims.

The secondary reference of Lin et al is cited here solely for the inclusion of an antigenic compound, and fails to cure the deficiencies of the combined teachings of Zong and Morahan as discussed above. Lin et al. does not teach that an adjuvant composition with the weight/size characteristics provided in the pending claims is suitable for human use. Instead, Lin et al. at best only discloses polynucleotide adjuvant compositions of smaller sizes (5-8S).

The arguments set out above with respect to the rejection of the claims based on the combination of Zong et al. (as evidenced by Lin) and Morahan et al. applies with equal force here. Specifically, one would not be able to predict with any expectation of success in view of the art cited above that a polynucleotide adjuvant having the size and molecular weight characteristics recited in the claims would provide for a composition that was suitable for human use.

First, one would not look to Morahan for guidance on modification of the compositions of Zong, since the interferon-inducing effect of the Poly IC compositions of Morahan is suppressed by human sera and are rapidly degraded in human plasma, as evidenced by De Clercq. Rather, one would look to PIC-containing compositions, which were developed to address the stability issues of Poly IC. When the ordinarily skilled artisan turned to the art relating to PIC-containing compositions (e.g. Gatmaitan et al., Levy et al. and Shu et al., discussed above), she would find that this art teaches that PIC-containing compositions with smaller molecular weights/sizes are less toxic. Thus the ordinarily skilled artisan would predict

that providing PIC-containing compositions of *lower* molecular weight/size would provide a polynucleotide adjuvant suitable for human use and, furthermore, that compositions having an *larger* molecular weight/size, such as encompassed by the present claims, would result in toxicity that renders the composition unsuitable for human use. Instead, and unexpectedly, the claimed polynucleotide adjuvant is *larger* than that described in the cited art *and yet, unexpectedly, provides for a balance of immunogenicity and toxicity that renders the claimed composition suitable for use in humans.* Thus, *increasing* the molecular size and weight of the claimed compositions is not "a technique [that] has been used to improve one device, and a person of ordinary skill in the art would recognize that it would improve similar devices in the same way."[23]

In view of the above, one of ordinary skill in the art would not be able to predict with any expectation of success that combining an antigenic composition such as that in Lin with compositions of the molecular weight size of Zong et al. or greater would provide for an adjuvant composition that was suitable for use in humans. Simply put, such compositions would be expected to be too toxic. Rather, one would gravitate towards PICKa compositions with smaller molecular weights/sizes.

Reconsideration and withdrawal of this rejection of the claims is respectfully requested.

DOUBLE PATENTING REJECTIONS

The following four obviousness-type double patenting rejections have been made:

- Claims 27, 31-32, 34-38 and 52-78 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 1 of copending Application Serial No. 11/331,575.
- Claims 27-45 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 1 of copending Application Serial No. 11/331,839.

[23] *KSR,* slip op. at 13. (citations omitted)

- Claims 27-45 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 9 of copending Application Serial No. 12/160,853.[24]
- Claims 27-45 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 2 of copending Application Serial No. 12/160,584.

The Examiner noted that timely filed Terminal Disclaimers (TDs) in compliance with 37 C.F.R. §1.321(c) or 1.321(d) was provided with the previous response. However, the TDs were refused entry on the assertion that the attorney who executed the TDs is not of record. During the interview, Applicants' representative presented documents establishing they have an executed Power of Attorney from NewBiomed PIKA Pte Ltd, the assignee of the above-referenced application, further that the inventor has assigned his rights to this same entity. Applicants noted that the Filing Receipt indicated that Power of Attorney had been assigned to Applicants' counsel's Customer Number.

Applicants have resubmitted the Terminal Disclaimers along with the executed Power of Attorney.

Withdrawal of this rejection is respectfully requested.

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[24] The Applicants submit that Application Serial No. 12/160,853 is unrelated to the pending application. However, the Applicants note that Application Serial No. 12/160,583 does have a common inventor and common assignee with the pending application. The Applicants assume that the Examiner transposed numbers in the course of drafting this rejection; accordingly, they will treat the obviousness-type double patenting rejection as being over Application Serial No. 12/160,583.

CONCLUSION

Applicant submits that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, please telephone the undersigned at the number provided. The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, order number NBMP-001(SP).

Respectfully submitted,
BOZICEVIC, FIELD & FRANCIS LLP

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Enclosure(s):

- Exhibits:
  - Exhibit A: De Clercq (1979) "Degradation of Poly(inosinic acid) – poly(cytidylic acid) [$(I)_n$ $(C)_n$] by Human Plasma"· *Eur. J. Biochem.* 93:165-172.
  - Exhibit B: Gatmaitan et al. (1980) "Modified Polyriboinosinic-Polyribocytidylic Acid Complex: Induction of Serum Interferon, Fever, and Hypotension in Rabbits" Antimicrobial Agents and Chemotherapy 17:49-54.
  - Exhibit C: Levy et al. (1981) "Interferon Induction in Primates by Stabilized Polyriboinosinic Acid-Polyribocytidylic Acid: Effect of Component Size" Infect. Immun. 34:416-421.
  - Exhibit D: Shu et al. (1989) "Biological functions and application of Poly I:C" *Shanxi Journal of Medicine* 18(10):40-42.
- Terminal Disclaimers over 11/331,575, 11/331,839, 12/160,584, 12/160,583.
- Power of Attorney
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